Docket No. 46745 (1758)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| APPLICANT: | J. Weidanz, et al. | | |
| SERIAL NO.: | 08/813,781 | EXAMINER: | M. Lubet |
| FILED: | March 7, 1997 | GROUP: | 1644 |
| FOR: | FUSION PROTEINS COMPRISING BACTERIOPHAGE COAT PROTEIN AND A SINGLE-CHAIN T CELL RECEPTOR | | |

DECLARATION OF JON A. WEIDANZ
UNDER 37 C.F.R. §1.132

Dear Madam:

1. I, Jon A. Weidanz declare and say that I am a resident of the United States. My residence address is 820 S.W. 141 Avenue, Miami, Florida 33184.

2. I hold a B.A. degree that I received from West Virginia University. I further hold a Ph.D. degree which I received from the University of Alabama while working in the laboratory of Dr. Lennart Roden. I am currently a Senior Scientist at Sunol Molecular Corporation 2810 North Commerce Parkway, Miramar Florida 33025. I am an expert in the fields of immunology, biochemistry, bacteriology, protein chemistry and molecular biology. My *curriculum vitae* is attached, and illustrates my expertise and experience in these and other areas.

3. I am a co-inventor of claims 1, 2, 4, 7, 8, 14, 67, 69, 71 and 72 in the above-identified patent application (subject application). I personally performed and/or assisted in research leading to the claimed invention.

4. I read the Office Action dated March 10, 2000 in the application. I understand from that Office Action that the Examiner rejected the claims on grounds that the claims are obvious.

5. I have been asked to address whether the T cell receptor (TCR) fusion protein encoded by a construct called pKC44 in the subject application effectively positions the V-α and V-β regions to form an antigen binding pocket. I have been further asked to address whether the TCR fusion protein encoded by pKC44 binds relevant antigen and/or stimulates T cells specific for the relevant antigen.

6. It is my understanding that a research article I co-authored entitled *Display of Functional αβ single-chain T-cell Receptor Molecules on the Surface of Bacteriophage* (Weidanz, J. et al. *J. Immunol. Methods* 221: 59 (1998); hereinafter "Weidanz et al.") shows that the pKC44 construct effectively positions the V-α and V-β regions to form an antigen binding pocket. I also understand that Weidanz et al. shows that the TCR fusion protein encoded by the pKC44 construct binds relevant antigen. A copy of Weidanz et al. is attached to this Declaration as **Appendix A**.

8. For example, Figure 4A of Weidanz et al. shows cellular inhibition assays in which a recombinant bacteriophage (called "scTCR/p8") inhibits interleukin 2 (IL-2) production by $IA^d$/OVA stimulated D011.10 T hybridoma cells. More specifically, Figure 4A shows that the scTCR/p8 bacteriophage includes a TCR fusion protein that effectively positions D011.10 type V-α and V-β regions to form a good antigen pocket. Figure 4A also shows that the antigen binding pocket of the TCR fusion protein of the phage bound OVA peptide, thereby competing with and reducing stimulation by the D011.10 hybridoma cells.

9. **The TCR fusion protein of the scTCR/p8 bacteriophage disclosed by Weidanz et al. is the same fusion protein encoded by the pKC44 construct.** In particular, sequence encoding the pKC44 TCR fusion protein was used to make the scTCR/p8 bacteriophage as follows.

10. The pKC44 construct was treated with *Sfi I* and *Xma I* restriction enzymes to release sequence encoding the fusion protein from the construct. That sequence was used to make an intermediate construct called pKC51. Methods for making and using pKC44 and pKC51 are disclosed throughout the subject application. For example, see Figure 3 and Example 1 of the subject application. As disclosed, the pKC44 and pKC51 constructs encode the same TCR fusion protein. See Figure 3A and Figure 3C for more information.

11. The pKC51 construct was used to make the scTCR/p8 bacteriophage along lines described throughout the subject application. For example, see Examples 14-15 at pages 65-72 (describing making and using bacteriophage expressing TCR fusion proteins). Related methods are disclosed in Weidanz et al. at pages 62-63 (showing production of bacteriophage bearing TCR). Accordingly, the TCR fusion protein encoded by pKC44, pKC51, and the scTCR/p8 bacteriophage are identical.

12. As I understand it, Weidanz et al. provides examples showing that the pKC44 TCR fusion protein effectively positions the V-α and V-β regions to form a binding pocket that binds specific antigen ie., the OVA peptide.

13. For example, Figure 4B of Weidanz et al. shows that the scTCR/p8 phage (having the same TCR fusion protein as pKC44) did not inhibit IL-2 production by $IA^d$/HSV-1 peptide stimulated gD12 T hybridoma cells. That is, the TCR fusion protein of the scTCR/p8 phage bound the OVA peptide but did not bind an unrelated peptide (HSV-1) very effectively.

14. As also understood, Weidanz et al. shows that the TCR fusion protein encoded by the pKC44 construct binds specific antigen in the correct context ie., with an appropriate MHC molecule.

15. For example, Figure 5 of Weidanz et al. shows that the scTCR/p8 phage (having the same TCR fusion protein as pKC44) binds cells expressing the OVA peptide in the context of the appropriate MHC molecule. More particularly, Figure 5A shows effective binding between the scTCR/p8 phage and NDO.B5 cells (engineered to express OVA peptide in the context of $IA^d$ MHC molecule). However, Figure 5A shows that good binding was not observed between the NSO cells (no expressed OVA peptide or MHC molecule) and the scTCR/p8 phage.

16. Accordingly, Weidanz et al. shows that the pKC44 TCR fusion protein effectively positions the V-α and V-β regions to form a binding pocket that binds specific antigen ie., the OVA peptide. The article further shows that the pKC44 fusion protein bound the OVA peptide antigen specifically and in the context of the correct MHC molecule.

17. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

6/23/2000
Date

Jon A. Weidanz

138840

# CURRICULUM VITAE



**Name**
Jon A. Weidanz
**Date and Place of Birth**
21st of December, 1962; Washington, D.C.
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**Home Address**
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**Work Address**
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**Current Position**
Senior Scientist
Program Leader, Cancer Therapeutics
Sunol Molecular Corporation

## EDUCATION (in reverse chronological order)

| Institution and Location | Degree | Years | Field of Study |
|---|---|---|---|
| University of Alabama at Birmingham, Birmingham, Alabama | Ph.D. | 1987-1992 | Molecular Biology |
| University of Alabama at Birmingham, Birmingham, Alabama | M.P.H. | 1985-1987 | Epidemiology |
| West Virginia University, Morgantown, West Virginia | B.S. | 1981-1985 | Biology (cum laude) |

**Ph.D. Dissertation Project:** Hexosamine Metabolism and its Regulation in the Human Erythrocyte and the Malaria Parasite, *Plasmodium falciparum*.

## CONTINUING EDUCATION COURSES

Completed several courses in a Master of Business Administration program

## RESEARCH AND PROFESSIONAL EXPERIENCE (in reverse chronological order)

| | |
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| 1999- | Senior Scientist, Sunol Molecular Corp. |
| 1996-1999 | Research Scientist, Sunol Molecular Corp. |
| 1996 | Co-founder, Sunol Molecular Corp. |
| 1992-1996 | Research Scientist, Dade International/Baxter Diagnostics, Inc. |
| 1993-1994 | Adjunct Assistant Professor, Department of Medical Laboratory Sciences, Florida International University |
| 1987-1992 | Graduate Research Assistant, Department of Microbiology and the Division of Geographic Medicine, University of Alabama at Birmingham |

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|---|---|
| 1986-1987 | Graduate Research Assistant, Department of Microbiology, University of Alabama at Birmingham |
| 1985-1986 | Graduate Research Assistant, School of Public Health, University of Alabama at Birmingham |
| 1984-1985 | Undergraduate Research Assistant, Department of Biochemistry, West Virginia University |

SCHOLASTIC ACTIVITIES AND HONORS (in reverse chronological order)

NIH Molecular Biology Pre-doctoral Training Grant – (1987-1989)
President, Student Government, School of Public Health- (1986)
School-wide Representative "The Student Society for International Health Promotion"-(1986)
Participant in the Biology Honors Program, West Virginia University (1983-1985)

MEMBERSHIPS

American Society for Microbiology
American Association of Immunologists

COMMITTEES

Panel Member of RAID (Rapid Access to Intervention Development) study section NCI Developmental Therapeutics Program (1998-2000)

Ad Hoc Member for the Committee on Militarily Critical Technologies, Biotechnology Section, Department of Defense, United States of America (1995-1996)

GRANTS

AWARDED

NIH/SBIR: PHASE I (1R43CA88615-01) 06/01/00-05/31/01
**P.I. Jon A. Weidanz**
Title: T cell receptor-based immunotherapeutics for cancer.

NIH/SBIR: PHASE I (1R43CA76856-01) Jan-Jul. 1998
**P.I. Jon A. Weidanz**
Title: Development of recombinant bispecific anti-tumor molecules.

PENDING

NIH/RO1: (1RO1 CA84477-01) 01/01/00-12/31/04
**P.I. Jon A. Weidanz**
Title: TCR-based bispecific molecules retarget effector cell function.

SPEAKING INVITATIONS

I have given seminars at the Annual Meeting for the American Association of Immunologists (Seattle), the University of Texas (San Antonio), Texas Tech University (Amarillo), the University of Miami, Louisiana State University (Shreveport), Florida Atlantic University, the University of Wisconsin (Madison), the University of Maryland, the University of Nebraska Medical Center (Omaha), and at Dupont-Merck.

## TEACHING EXPERIENCE

Tutor for Cellular and Molecular Biology, 1988-1990
Thesis Committee Member, Department of Medical Laboratory Sciences, Florida International University, 1993-1994
Supervise undergraduate research assistants, Sunol Molecular Corp. 1996-1999

## RECENT PUBLICATIONS (in reverse chronological order)

J.A. Weidanz and K.F. Card. Construction and Expression of Covalently Linked scTCR/scFv Bispecific Molecules. Manuscript in preparation.

J. A. Weidanz, K. F. Card, Ana Edwards, E. Perlstein, H.C. Wong. (1998) Display of functional αβ sc T cell receptor molecules on the surface of bacteriophage. Journal of Immunological Methods, 221: 59-76.

C. L. Casispit, P. Chavaillaz, K. Arbuthnott, J. A. Weidanz, J. Jiao, R. Tal, and H.C. Wong. (1998) Improving antibody affinity using molecular modeling and site directed mutagenesis. Protein Science, 7: 1-10.

J. A. Weidanz, P. Campbell, D. Moore, L.J. DeLucas, L. Rodén, J. N. Thompson, and A.C. Vezza. (1996) N -Acetylglucosamine kinase and N-acetylglucosamine 6-phosphate deacetylase in normal human erythrocytes and *Plasmodium faciparum*. British Journal of Haematology. 95: 645-653.

J. A. Weidanz, P. Campbell, D. Moore, L. DeLucas, l. Rodén, and A.C. Vezza. (1995) Glucosamine 6-phosphate deaminase in *Plasmodium falciparum*. British Journal of Haematology. 91: 578-586.

J. A. Weidanz, P. Campbell, D. Moore, L. DeLucas, L. Rodén, and A. C. Vezza. (1995) Glucosamine 6-phosphate deaminase in normal human erythrocytes. British Journal of Haematology. 91: 72-79.

## PATENTS

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Sherman, L.A., Card, K., and Weidanz, J.A. T cell receptors from HLA-A2 transgenic mice specific for peptides of human p53. 2000 (Patent submitted).

Weidanz, J.A., Wittman, V., Wong, H., and Taylor, D. Transgenic non-human animals capable of producing heterologous T cell receptors. 2000. (Patent submitted).

Wittman, V., Rhode, P., Weidanz, J.A., Wong, H., Card, K., Burkhardt, M. and Taylor, D. Methods of Identifying Compounds that Modulate an Immune Response. 1999. (Patent Submitted).

J. A. Weidanz and K.F. Card. Construction of Multivalent scTCR Complexes and Uses Thereof. 1998.

J. A. Weidanz, K.F. Card, L. Sherman, N. Klinman, and H.C. Wong. Bispecific scTCR-sFv hybrid molecules. 1998. U.S.S.N. 60/105,164).

J. A. Weidanz, K. F. Card, and H. C. Wong. Fusion Proteins Comprising sc-TCR and an Immunoglobulin Light Chain Constant Region. 1997. U.S.S.N. 08/943,086.

J. A. Weidanz, K. F. Card, and H. C. Wong. Fusion Proteins Comprising Bacteriophage Coat Protein and a Single-Chain T Cell Receptor. 1997. U.S.S.N. 08/813,781.

H. C. Wong, P. R. Rhode, J. A. Weidanz, S. Grammer, A. Edwards, and P.-A. Chavaillaz. MHC Complexes and Uses Thereof. 1994. US/08/382,454.

ABSTRACTS

Weidanz, J., Thomson, E., Chavaillaz, P., Wwittman, V., Wong, H., and Card, K. T cell receptor based immunotherapeutics. Amer. Assoc. Imm. Seattle, 2000. (Oral Presentation).

Morjana, N., Tal, R., Weidanz, J. A. and DeMarco, C. The reversible denaturation of cardiac Troponin-I. ASBMB, 1995.

Weidanz, J. A., Campbell, P., Moore, D., DeLucas, L., Roden, L. and Vezza, A.C. Characterization of N-acetylglucosamine 6-phosphate deacetylase and glucosamine 6-phosphate deaminase from *Plasmodium falciparum* and normal human eythrocytes. Am. Fed. Clin. Res., 40(2), 1992.

Weidanz, J. A., Campbell, P., Moore, D., Roden, L. and Vezza, A.C. Isolation of the *Plasmodium falciparum* glucosamine 6-phosphate (GlcN-6-P) deaminase which is distinctly different from the host eythrocyte enzyme. FASEB, 6(5):5578, 1992.

Weidanz, J. A., Campbell, P., Roden, L. and Vezza, A.C. Glucosamine 6-phosphate deaminase and N-acetylglucosamine 6-phosphate deacetylase from normal and *Plasmodium falciparum* infected eythrocytes. Am. Soc. of Trop. Med. and Hyg., 45:128, 1991.

van der Heyde, H.C., Weidanz, J. A., Bucy, R.P., Greene, B.G. and Weidanz, W.P. Changes in splenic T cell populations during experimental murine *Plasmodium chabaudi adami* malaria. Twenty-Sixth Joint Conference on Parasitic Diseases, U.S.-Japan Meeting. Birmingham, Alabama. Oral presentation by Dr. Weidanz. 1991.

Weidanz, J. A., Campbell, P., Moore, D., DeLucas, L., Roden, L. and Vezza, A.C. The identification, purification and biochemical characterization of N-acetylglucosamine 6-phosphate deacetylase and glucosamine 6-phosphate deaminase from human erythrocytes and the malaria parasite *Plasmodium falciparum*. Twenty-Sixth Joint Conference on Parasitic Diseases, U.S.-Japan Meeting. Birmingham, Alabama. Oral presentation by Jon Weidanz. 1991.

van der Heyde, H.C., Weidanz, J. A., Bucy, R.P., Greene, B.M. and Weidanz, W.P. T gamma delta cells in murine malaria, *Plasmodium chabaudi adami*. Am. Fed. Clin. Res., 39(2), 1991.

**Weidanz, J. A.**, van der Heyde, H.C. and Vezza, A.C. Differential regulation of early (KAHRP) and late (gp200) genes in the asexual stage of *Plasmodium falciparum.* Am. Fed. Clin. Res., 39(2), 1991.

**Weidanz, J. A.** and Vezza, A.C. Biosynthesis and glycosylation of the *Plasmodium falciparum* gp195 protein. Am. Fed. Clin. Res., 38(2), 1990.